REMARKS

By way of the instant preliminary amendment, Applicants have added claims 96-99. Support for these claims is found in the specification, e.g., at pages 9-10 and 29-30. Claims 2-7, 23-24, 33-35, 43-51, 53-60, 62-68, 70-74, 76-86, and 88-95 have been amended to add references to new claims (i.e., claims 96-99) and to use appropriate articles. Claims 8-21, 26-31 and 36-41 have been canceled without prejudice. No new matter has been introduced by the foregoing amendments.

In the Office Action dated December 31, 2002, the Examiner has set forth a requirement for restriction under 35 U.S.C. §121, alleging that the subject matter defined by the claims of the present invention represents the following fifteen separate and distinct inventions:

Group I. Claims 1-2, 4-5, 7-9, 11-13, 15-16, 22-23, 25-28, 42-43, 45-51, 75-76, 78-79, 81-88, 90-91, and 93-95, only as drawn to a method of modulating the expression of a genetic sequence, wherein said sequence comprises an ORF having an ATG corresponding to an authentic translation site, said method comprising removing one or more ATG triplets, classified in class 435, subclass 91.42.

Group II. Claims 1, 3-5, 7-9, 11-12, 14-16, 32-33, 35-38, 42-43, 45-51, 75, 77-79, 81-87, 89-91, and 93-95, only as drawn to a method of modulating the expression of a genetic sequence, wherein said sequence comprises an ORF having an ATG corresponding to an authentic translation site, said method comprising introducing one or more ATG triplets, classified in class 435, subclass 91.42.

Group III. Claims 1-2, 4, 6-8, 10-11, 17-18, 20-22, 24-25, 29-31, 42, 44-51, 75-76, 78, 80-88, 90, and 92-95, only as drawn to a method of modulating the expression of a genetic sequence, wherein said sequence comprises an ORF having an ATG corresponding to an authentic translation site, said method comprising removing one or more AUG triplets, classified in class 435, subclass 91.42.

Group IV. Claims 1, 3-4, 6-8, 10-11, 17, 19-21, 32, 34-35, 39-42, 44-51, 75, 77-78, 80-87, 89-90, and 92-95, only as drawn to a method of modulating the expression of a genetic sequence, wherein said sequence comprises an ORF having an ATG corresponding to an

authentic translation site, said method comprising introducing one or more AUG triplets, classified in class 435, subclass 91.42.

Group V. Claims 1-2, 7, 9, 11-13, 16, 22, 26, 28, 42-43, 45-51, 75-76, 81-88, and 93-95, only as drawn to a method of modulating the expression of a genetic sequence, wherein said sequence comprises an ORF having an ATG corresponding to an authentic translation site, said method comprising removing one or more GTG triplets, classified in class 435, subclass 91.42.

Group VI. Claims 1, 3, 7, 9, 11-12, 14, 16, 32, 3-36, 38, 42-43, 45-51, 75, 77, 81-87, 89, and 93-95, only as drawn to a method of modulating the expression of a genetic sequence, wherein said sequence comprises an ORF having an ATG corresponding to an authentic translation site, said method comprising introducing one or more GTG triplets, classified in class 435, subclass 91.42.

Group VII. Claims 1-2, 7, 10-11, 17-18, 21-22, 29, 31, 42, 44-51, 75-76, 81-88, and 93-95, only as drawn to a method of modulating the expression of a genetic sequence, wherein said sequence comprises an ORF having an ATG corresponding to an authentic translation site, said method comprising removing one or more GUG triplets, classified in class 435, subclass 9142.

Group VIII. Claims 1, 3, 7, 10-11, 17, 19, 21, 32, 35, 39, 41-42, 44-51, 75, 77, 81-87, 89, and 93-95, only as drawn to a method of modulating the expression of a genetic sequence, wherein said sequence comprises an ORF having an ATG corresponding to an authentic translation site, said method comprising introducing one or more GUG triplets, classified in class 435, subclass 91.42.

Group IX. Claims 52-53 and 55-60, drawn to isolated nucleic acid comprising ATG, classified in class 536, subclass 23.1.

Group X. Claims 52 and 54-60, drawn to isolated nucleic acid comprising AUG, classified in class 536, subclass 23.1.

Group XI. Claims 61-68, drawn to genetic construct, classified in class 435, subclass 320.1.

Group XII. Claims 69-70 and 74, drawn to method for modulating expression of a genetic sequence comprising creating or removing one or more ATG pseudo-translation initiation triplets, classified in class 435, subclass 91.4.

Group XIII. Claims 69, 71, and 74, drawn to method for modulating expression of a genetic sequence comprising creating or removing one or more GTG pseudo-translation initiation triplets, classified in class 435, subclass 91.4.

Group XIV. Claims 69, 72, and 74, drawn to method for modulating expression of a genetic sequence comprising creating or removing one or more AUG pseudo-translation initiation triplets, classified in class 435, subclass 91.4.

Group XV. Claims 69 and 73-74, drawn to method for modulating expression of a genetic sequence comprising creating or removing one or more GUG pseudo-translation initiation triplets, classified in class 435, subclass 91.4.

The Examiner alleges that Groups I-XV are drawn to products or methods which relate to sequences which are chemically, biologically, and structurally different and distinct from each other. Therefore, the Examiner states that these groups do not render obvious each other, and are patentably distinct. The Examiner requires Applicants to elect a single invention directed to a product or method drawn to one specific sequence. The Examiner states that this restriction to examination of a single sequence is due to the now very high and undue burden for examining more than one sequence which is caused by the continued exponential increase of size of the sequence databases to be searched for each sequence, resulting in a corresponding increase in computer search time and examiner time for reviewing the computer search results.

The Examiner also alleges that the inventions of Groups I-VIII and XII-XV are different and distinct from each other. Specifically, the Examiner contends that the methods of each of these groups comprise steps which are not required for in the methods of the other groups. The operation, function and effects of the methods of these groups are different and distinct from each other.

The Examiner further alleges that the products of Groups IX-XI are chemically,

biologically, and functionally distinct from each other. The Examiner indicates that the products of these groups are capable of supporting separate patents.

In addition, the Examiner alleges that the inventions of Groups IX-XI are unrelated to Groups I-VIII or XII-XV, allegedly because the products of Groups IX-XI are not used in, or produced by, the methods of Groups I-VIII or the methods of Groups XII-XV.

In order to be fully responsive to the Examiner's requirement for restriction, Applicants provisionally elect to prosecute the subject matter of Group II, directed to methods of modulating the expression of a genetic sequence by introducing one or more ATG triplets. In view of the preliminary amendment to the claims, claims 1, 3-5, 7, 32-33, 35, 42-43, 45-51, 75, 77-79, 81-87, 88-91, 93-95, and new claims 96 and 98 are elected for further prosecution. Applicants reserve the right to file one or more divisional applications directed to the non-elected subject matter in this application. However, pursuant to 37 C.F.R. §§ 1.111 and 1.143, Applicants hereby traverse the Examiner's requirement for restriction and request reconsideration thereof in view of the following remarks.

An Examiner's authority to require restriction is defined and limited by statute:

> If two or more <u>independent and distinct</u> inventions are claimed in one application, the Commissioner may require the application to be restricted to one of the inventions.

35 U.S.C. § 121, first sentence (emphasis added). The implementing regulations of the Patent and Trademark Office include the mandate that restriction is appropriate only in cases presenting inventions which are both independent <u>and</u> distinct, 37 C.F.R. §§1.141-142. Without a showing of independence and distinctness, a restriction requirement is unauthorized.

In the present application, the claims which the Examiner has grouped separately are not "independent and distinct" so as to justify the restriction requirement. Applicants respectfully submit that these groups are all different aspects of a single invention. More specifically, it is the unique recognition of the present invention that gene expression can be modulated by altering the number of sequence elements corresponding to pseudo-translation initiation sites, i.e., RUG or RTG (wherein R is A or G), within the 5' leader sequence upstream of the authentic translation initiation site. According to the present invention, elevated expression of a genetic sequence can be achieved by removing or destroying the RTG or RUG triplets in the upstream sequence; and expression can be reduced by introducing or creating pseudo-translation initiation sites in the upstream sequence. Therefore, Groups I, III, V, VII, and XII-XV are clearly related to each other, as the methods of these groups all relate to modulating gene expression by removing or destroying one or more pseudo-translation initiation sites. Groups II, IV, VI, VIII and XII-XV are also related to each other, as the methods of these groups all relate to modulating gene expression by introducing or creating one or more pseudo-translation initiation sites. Furthermore, Groups I-VIII and XII-XV are related to each other, as the methods of these groups all relate to methods of modulating gene expression by altering the number of pseudo-translation initiation sites within the leader sequence of a gene. In addition, Groups IX-XI are directed to isolated nucleic acid molecules or genetic constructs which contain a predetermined number of pseudo-translation initiation sites such that a genetic sequence can be expressed at a pre-determined level. Clearly, the nucleic acid molecules and genetic constructs of Groups IX-XI are linked to the methods of Groups I-VIII and XII-XV under a single inventive concept. Therefore, Groups I-XV are not independent and distinct as the Examiner has alleged.

Applicants further submit that the courts have recognized that it is in the public interest to permit applicants to claim several aspects of their invention together in one application, as the applicants have done herein. The CCPA has observed:

> We believe the constitutional purpose of the patent system is promoted by encouraging applicants to claim, and therefore to describe in the manner required by 35 U.S.C. §112 all aspects as to what they regard as their invention, regardless of the number of statutory classes involved.

In re Kuehl, 456 F.2d 658, 666, 117 U.S.P.Q. 250, 256 (CCPA 1973). This interest is consistent with the practical reality that a sufficiently detailed disclosure supporting claims to one aspect of an invention customarily is sufficient to support claims in the same application to other aspects of the invention.

The Examiner also states that the inventions have acquired a separate status in the art as evidenced by the separate classification and recognized divergent subject matter and would require independent searches. Thus, the Examiner concludes that restriction for examination purposes is proper.

Reliance on the supposed classification of the groups of claims does not establish independence and distinctness. The classification system has no statutory recognition as evidence of whether inventions are independent and distinct. The classification system is instead an aid in finding and searching for patents.

The classification system is also an unreliable basis for requiring restriction between claims to the various aspects of applicants' unitary invention, because the system exhibits considerable overlap in technical definitions. In particular, the definitions of classes and subclasses in the classification system do not prevent the Examiner from basing patentability

decisions, as to claims assigned to one group, on patent references found in the classes or subclass(es) with which he associated another group of claims.

Furthermore, the classification system is a poor basis for requiring restriction between related aspects of an invention because classifications and definitions change over time. Thus, a classification that might have seemed to support restriction at a given time could change, thereby casting a shadow over the propriety of the restriction requirement later on during the term of the patents issuing from parent and divisional applications. Indeed, classifications seem largely to change in response to considerations of administrative convenience, and often in response to nothing more than growth in the number of patents in a given class or subclass. These considerations have nothing to do with whether the subject matter of patents assigned to different classifications is "independent and distinct" as those terms are used in 35 U.S.C. §121, which fact proves that basing restriction requirements on the classification system is improper.

Applicants respectfully suggest that in view of the continued increase of official fees and the potential limitation of an applicant's financial resources, a practice which arbitrarily imposes restriction requirements may become prohibitive and thereby contravene the constitutional purpose to promote and encourage the progress of science and the useful arts. Moreover, under the regulatory changes as a consequence of the General Agreement on Trade and Tariffs (GATT), applicants are required to conduct simultaneous prosecution, as here, requiring excessive filing costs or otherwise compromise the term of related patent assets.

It is vital to all applicants that restriction requirements issue only with the proper statutory authorization, because patents issuing on divisional applications which are filed to prosecute claims that the Examiner held to be independent and distinct can be vulnerable to

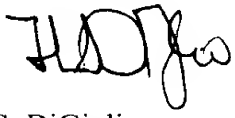
legal challenges alleging double patenting. The third sentence of 35 U.S.C. §121, which states that a patent issuing on a parent application "shall not be used as a reference" against a divisional application or a patent issued thereon, does not provide comfort to applicants against such allegations. The Court of Appeals for the Federal Circuit has declined to hold that § 121 protects a patentee from an allegation of same-invention double patenting, Studiengesellschaft Kohle GmbH v. Northern Petrochemical Co., 784 F.2d 351, 355, 288 U.S.P.Q. 837, 840 (Fed. Cir. 1986). In Gerber Garment Technology Inc. v. Lectra Systems Inc., 916 F.2d 683, 16 U.S.P.Q. 2d 1436 (Fed. Cir. 1990), the court held that §121 does not insulate a patentee from an allegation of "obviousness-type" double patenting, and in fact affirmed the invalidation on double patenting grounds of a patent that had issued from a divisional application filed following a restriction requirement. Furthermore, it is far from clear that the step of filing a terminal disclaimer is available to resolve a double patenting issue that arises after the issuance of a patent on the divisional application.

All these considerations indicate that the imposition of a restriction requirement with inadequate authority can lead to situations in which an applicant's legitimate patent rights are exposed to uncertainty and even extinguished. Accordingly, to protect a patentee's rights and to serve the public interest in the legitimacy of issued patents, Applicants respectfully urge the Examiner not to require restriction in cases such as the present application wherein various aspects in a unitary invention are claimed.

Finally, Applicants respectfully submit that a determination to make the pending restriction requirement final must evidence the patentable distinctness of all defined fifteen groups, one from the other, as presented by the Examiner.

In view of the foregoing comments, it is respectfully urged that the Examiner reconsider and withdraw the requirement for restriction and provide an action on the merits with respect to all the claims.

Respectfully submitted,



Frank S. DiGiglio
Registration No. 31,346

SCULLY, SCOTT, MURPHY & PRESSER
400 Garden City Plaza
Garden City, New York 11530
(516) 742-4343

FSD/XZ:ab